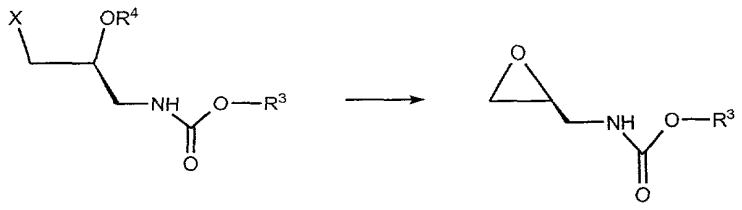
Scheme 6



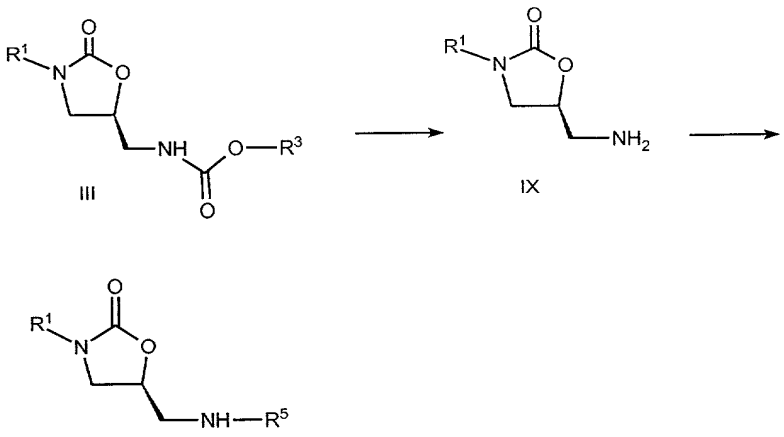
IV, R^4 = H
V, R^4 = C_1-C_6 alkylcarbonyl

II

an (S)-3-carbon amino alcohol (IV) or an (S)-secondary ester/protected alcohol (V). The (S)-epoxide (II) can be obtained by reaction of an (S)-secondary ester/protected alcohol (V) with a base, such as potassium or lithium t-butoxide, in a solvent, such as methanol. The (S)-epoxide can be isolated in crystalline form after chromatography. An (S)-epoxide (II) can be produced from a corresponding (S)-secondary alcohol (IV) by reaction with lithium t-butoxide in methanol at 20°C, as is set forth in Example 5. For an (S)-secondary alcohol (IV) or (S)-secondary ester/protected alcohol (V), it is preferred that R^4 is acetyl. For either an (S)-3-carbon amino alcohol (IV) or (S)-secondary ester/protected alcohol (V), X can be halogen, alkylsulfonyl, or arylsulfonyl, and preferably is Cl.

An (S)-oxazolidinone intermediate (III) is readily transformed to the corresponding pharmacologically active (S)-oxazolidinones (X) and (XI), as shown in Scheme 7. (S)-Oxazolidinone intermediate (III) first can be transformed to the

Scheme 7



X, R^5 = C_1-C_6 alkylcarbonyl or C_1-C_6 cycloalkylcarbonyl
XI, R^5 = C_1-C_6 alkylthiocarbonyl or C_1-C_6 cycloalkylthiocarbonyl

(S)-oxazolidinone free amine (IX). (S)-oxazolidinone free amine (IX) then is acylated with an appropriate acylating or thioacylating reagent, such as an activated acid, acyl halide, acyl anhydride, or dithioester, under acylation or thioacylation reaction conditions well known to those skilled in the art (see Examples 14 and 16, and WO 00/32599), to produce an (S)-oxazolidinone (X) or (XI) product, respectively.

Alternatively, the transformation from compound (III) to compound (X) or (XI) can be accomplished as a one pot process without isolating amine (IX). It is preferred that the acylating or thioacylating agent is selected from the group consisting of an acid anhydride of the structural formula $O(R^5)_2$, an activated acid of the structural formula R^5X, and a dithioester of the structural formula $R^5S(C=S)R^5$, wherein R^5 is C_1-C_6 alkylcarbonyl, C_1-C_6 cycloalkylcarbonyl, C_1-C_6 alkylthiocarbonyl, or C_1-C_6 cycloalkylthiocarbonyl, and X is halogen, alkylsulfonyl, or arylsulfonyl. It is preferred that the acylating agent or thioacylating agent is used in conjunction with a base, such as a tri(C_1-C_5 alkyl)amine. It is more preferred that R^5 is acetyl and X is Cl. Specifically, it is more preferred that the acylating reagent is an acyl anhydride, and most preferably the acyl anhydride is acetic anhydride.

General Methods and Definitions

Reagents were obtained from commercial sources and used without further purification. All temperatures are in degrees Centigrade. When solvent pairs are used, the ratios of solvents used are volume/volume (v/v). When the solubility of a solid in a solvent is used the ratio of the solid to the solvent is weight/ volume (wt/v). Reactions with moisture sensitive reagents were performed under a nitrogen atmosphere. Concentration of volumes was performed by reduced pressure rotary evaporation. Brine refers to an aqueous saturated sodium chloride solution. Chromatography (column and flash) refers to purification/separation of compounds expressed as (support/ eluent). It is understood that the appropriate fractions are pooled and concentrated to give the desired compound(s). High performance liquid chromatography (HPLC) analysis was performed using a Dionex DX-500 system with UV detection at 229 NM. Thin layer chromatography (TLC) was performed using 250 micron Analtech silica GF plates. CMR refers to C-13 magnetic resonance spectroscopy, chemical shifts are reported in ppm downfield from tetramethylsilane (TMS). NMR refers to nuclear magnetic resonance spectroscopy. ^{1}H NMR refers to proton nuclear magnetic resonance spectroscopy with chemical shifts reported in ppm downfield from TMS. $[\ I]^{22}{}_{D}$ refers to the angle of plane polarized light (specific optical rotation) at 25°C with the sodium D line (589 A). Mass spectromotry (MS) is expressed as m/e, m/z or mass/ charge unit and is obtained using electron impact (EI), chemical ionization (CI) or fast atom bombardment (FAB) techniques. $[M+H]^{+}$ refers to the positive ion of a parent plus a hydrogen atom. Retention time (RT) is in minutes and refers to the elution time of the compound after injection. IR refers to infrared spectroscopy. FTIR refers to Fourier Transform IR.